ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

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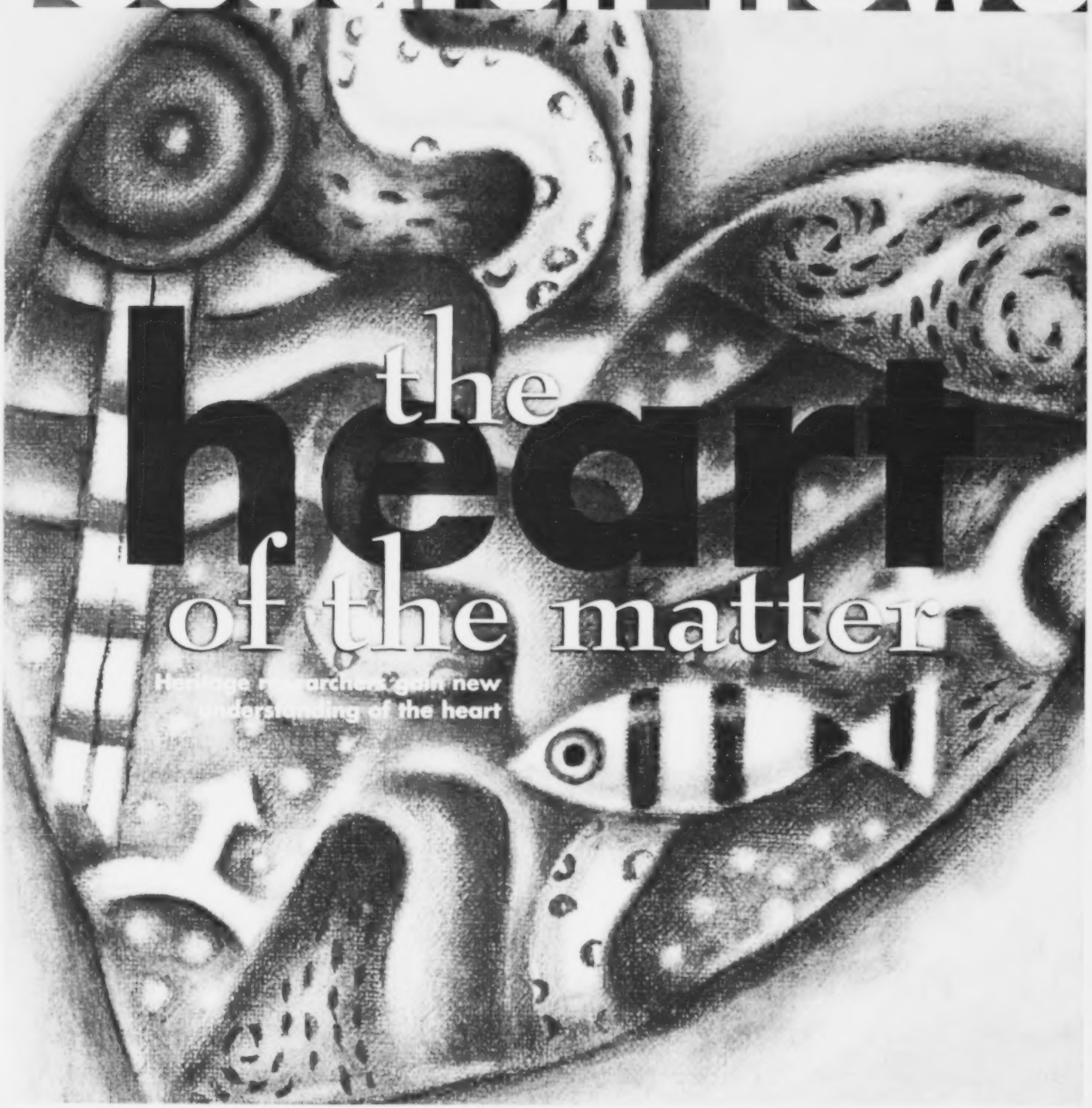
research news

FALL 2002



the heart of the matter

Heritage researchers gain new understanding of the heart

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AHFMR Mission

AHFMR supports a community of researchers who generate knowledge that improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund basic, patient and health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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Perhaps this challenge can be met. Drs. Armstrong and Sheldon have developed an innovative Alberta-based research training program called TORCH (Tomorrow's Research Cardiovascular Health Professionals). The two-year program is designed to combat a severe shortage of cardiovascular researchers in Canada. Launched in March 2002 by a consortium of partners including AHFMR, which will contribute up to $900,000, the program currently has 14 trainees studying cardiovascular-related issues at the universities of Alberta or Calgary.

TORCH matches students with mentors, and is open to a wide variety of health professionals, including physicians, nurses, basic scientists, and other paramedical personnel. The idea is to train these already highly skilled professionals in cardiovascular research.

Although great strides in diagnosis, treatment, and prevention have been made in the past two decades, major public health issues require the attention of dedicated and creative researchers. "There is so much we don't know--we're asking these bright young people to assess the limits of knowledge and use this as the starting point in the search for better ways to treat people with cardiovascular diseases," says Dr. Armstrong. He notes that TORCH is a systematic approach to training cardiovascular researchers, with funding for trainees, a core curriculum, commitment to career development, and exposure to job opportunities. "We're focused on research that crosses many different disciplines," he adds.

Dr. Colleen Norris is in the first group of TORCH trainees. She has a nursing degree and a Ph.D. in epidemiology. Her research will focus on nursing's role in improving outcomes for patients with cardiovascular disease.

"The treatments for heart disease try to control the chest pains and open up the circulation to the heart," Dr. Norris explains. "The big question in outcomes research is: Are we improving the day-to-day functional status of the patients so that they can get back to doing the things they enjoy?

"To fully understand the outcomes of care, it is necessary to understand the clinical picture of a patient with coronary artery disease, as well as the processes of care. This is where the transdisciplinary nature of TORCH is so important. TORCH trainees attend weekly seminars where various trainees from different disciplines and research backgrounds (basic science, clinical, and epidemiological) provide a piece of the patient puzzle. Whether it is from the nursing, pathophysiological, surgical, medical, pharmacological, or nutritional perspective, we try to put the pieces together. We either get a clearer understanding of the whole puzzle, or we see where further research is needed."

Dr. Paul Armstrong is a Professor in the Department of Medicine's Division of Cardiology at the University of Alberta. Dr. Robert Sheldon is a Professor in the Division of Cardiology at the University of Calgary. Dr. Colleen Norris is a post-doctoral fellow at the University of Alberta. The TORCH program is a Strategic Initiative in Health Research, one of 51 such projects announced by CIHR in 2002. The TORCH grant was provided in partnership with AHFMR, the CIHR Institutes of Circulatory & Respiratory Health and Gender & Health (which provided a $1.6 million grant), and the Heart and Stroke Foundation of Canada.

Biocom

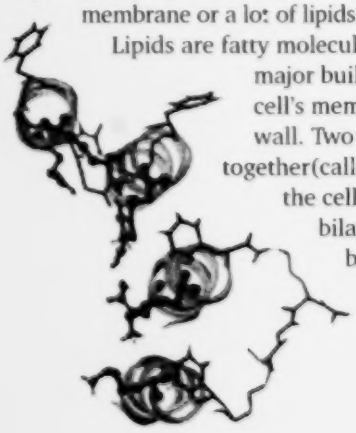
pictures worth many

If a picture is worth a thousand words, Dr. Peter Tieleman's computer-generated images must be worth hundreds of calculations. Dr. Tieleman couples physics and chemistry with high-powered computing to depict the structure and activity of molecules in the cells of biological systems.

"We build very detailed models of proteins and lipids," says Dr. Tieleman, a Heritage Scholar. "And then, using a very powerful computer, we try to determine how these lipids and proteins behave by simulating how they move." Based on these "molecular dynamics" simulations, "we try to draw conclusions about how lipids and proteins interact, what cell membranes look like at a detailed level, how they interact with drugs, and how ions are transported through cell membranes."

Better understanding of cell membrane structure will help develop more targeted and effective drugs for diseases such as cancer and cystic fibrosis, says Dr. Tieleman, who also holds a joint appointment in the Faculty of Medicine's Physiology and Biophysics Department at the University of Calgary.

Dr. Tieleman does all his work using computers, although he collaborates with colleagues who do experimental work on actual cells in the laboratory. His computer models start with well-understood physical and chemical properties of atoms that make up biological systems, such as carbon, oxygen, hydrogen, and nitrogen. Using that kind of knowledge, you can describe how a single molecule behaves by inputting mathematical calculations into the computer, he explains. "We take many of these molecules and see how they behave together, like a protein in solution or a drug in a [cell] membrane or a lot of lipids together."



Lipids are fatty molecules, which are the major building blocks of a cell's membrane, its thin outer wall. Two layers of lipids together(called a "bilayer") form the cell membrane. This bilayer gives the membrane its impermeability to substances circulating in the fluid outside the cells, substances which include water, sugar, and electrically charged ions such as sodium, potassium, chloride, and calcium. The cell membrane plays a key role in regulating biochemical activities in living organisms by either allowing or blocking the passage of ions into the cell.

Dr. Tieleman uses molecular-modelling software to draw the structure of a lipid molecule present in biological membranes. After he inputs the physical and chemical properties of the molecule, the computer program automatically builds the model of the cell membrane in three dimensions. His models and simulations complement and enhance the knowledge gained through laboratory experiments on actual cells. A lab experiment, for example, might produce eight pieces of experimental data that give researchers some idea of a cell's bilayer membrane structure, Dr. Tieleman says. In a computer model, "we can reproduce these eight pieces of experimental data, and at the same time show the much more complicated underlying picture of this very flexible membrane."

One of Dr. Tieleman's projects involves investigating a compound called pentachlorophenol, a hazardous wood preservative. It bioaccumulates in the environment, and likely also in the cell membranes of living organisms. Dr. Tieleman uses pentachlorophenol as a test molecule to model how molecules introduced into a biological system are distributed in cell membranes. Understanding this mechanism could lead, for example, to rationally designed drugs that would kill or disable potentially deadly *E. coli* bacteria, the microbe that contaminated water in the Walkerton tragedy. Laboratory experiments have shown that the *E. coli* protein and its parts form a pore, a hole in the bacte-

puting

thousands of words

ria's cell membrane that allows nutrients and ions to move in and out of the cell. "But the [computer] simulations can tell you what kind of molecules can go through at which rates, and why certain molecules are blocked while others aren't blocked," Dr. Tieleman notes.

Biocomputing techniques can also assist in examining how ion channels in cell membranes are regulated. Ion channels are large proteins that form the gated pathways through the cell membrane. These channels open and close in response to electrochemical stimulation by ions circulating in the fluid outside the cell. Dr. Tieleman says that computer simulation might be able to show us the three-dimensional structure of these ion channels and where certain molecules bind to the channel in order to allow or block the passage of ions. That knowledge could help researchers develop new drugs to repair malfunctioning ion channels, which occur in diseases such as epilepsy, myotonia (uncontrolled muscle contraction), and cystic fibrosis.

Dr. Tieleman and his research group are also working on improving the accuracy and predictive capability of computer models of large, multi-drug-resistance (MDR) proteins. A protein called MDR1 P-glycoprotein, for example, is one of the main proteins that causes resistance to many cancer-treatment drugs. Another protein with similar structure is known as cystic fibrosis transmembrane regulator (CFTR)—the protein that is defective in cystic fibrosis. Modelling the structure and activity of these proteins within the cell membrane could lead to designer drugs that knock out the proteins causing drug resistance or repair the damaged CFTR protein.

Dr. Tieleman says he would be unable to do his research without the parallel processing power of 60 PCs with 120 microprocessors, all working together in what's called a "Beowulf cluster". He assigns animal names to all his computers, to keep them and the tremendous amount of data they generate organized. The Beowulf cluster is called Elk, while the server is Grizzly and assorted smaller computers are Lynx, Bobcat, and Badger.

Summarizing his interest in biocomputing, Dr. Tieleman says with a smile, "I guess I just like theory and dislike Petri dishes. This is an exciting time for computer applications in biochemistry."

Dr. Tieleman is a Heritage Medical Scholar and Assistant Professor in the Department of Biological Sciences at the University of Calgary. *His research is also funded by PENCE Inc. (the Protein Engineering Network of Centres of Excellence), NSERC (the Natural Sciences and Engineering Research Council of Canada), and the Canada Foundation for Innovation.*

Selected publications

Tieleman DP, Shrivastava IH, Ulmschneider MR, Sansom MS. Proline-induced hinges in transmembrane helices: possible roles in ion channel gating. *Proteins: Structure, Function, and Genetics* 2001 Aug 1;44(2):63-72.

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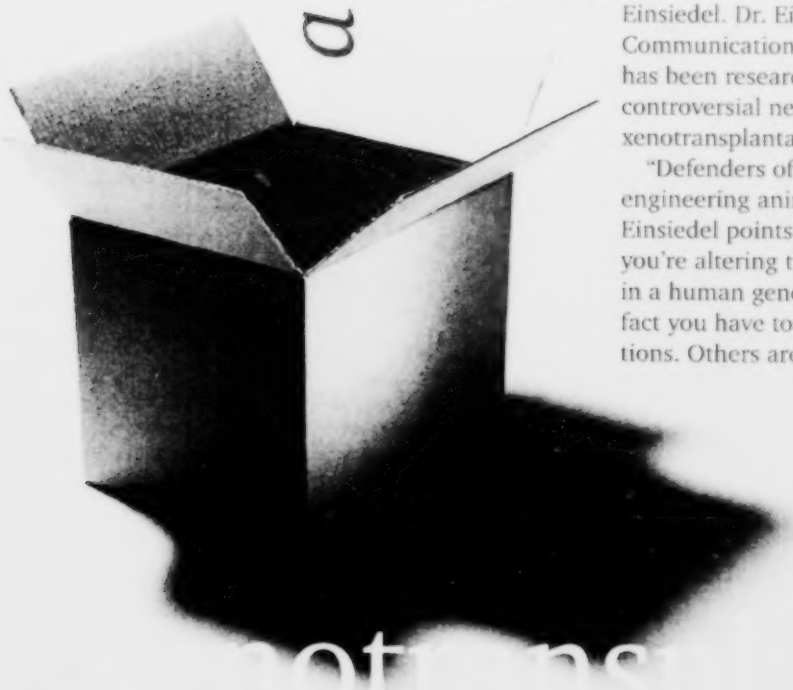
a Pandora's box?



In recent years, Canadian governments, scientists, doctors, and ethicists have been investigating the feasibility of transplanting cells, tissues, and organs from animals into humans. This has been tried often in the past but most patients died soon after the transplant, usually due to organ rejection. Currently, Canadian scientists are conducting preclinical studies to discover if inserting human genes into animals, such as pigs, would reduce the risks of rejection following transplantation. Experiments are also underway on cross-species animal transplants, such as from pigs to baboons.

Xenotransplantation (transplanting living cells, tissues, or organs from one species of animal to another) and the genetic modification of animals raise many complex legal, scientific, ethical, economic, and social issues, according to Heritage-supported researcher Dr. Edna Einsiedel. Dr. Einsiedel, a Professor in the Faculty of Communication and Culture at the University of Calgary, has been researching the public's role in assessing controversial new medical technologies, such as xenotransplantation.

"Defenders of animal rights question genetically-engineering animals solely to meet human needs," Dr. Einsiedel points out. "Some animal rights advocates say you're altering the nature of these animals when you put in a human gene. Some people have problems with the fact you have to keep these pigs in super-isolation conditions. Others are uncomfortable with the crossing of boundaries when you cross species. We've also had a history of virus transmission from animals to humans. Some of these viruses, like HIV and Ebola, have been quite virulent."

Dr. Einsiedel has been researching the public's role in assessing controversial new medical technologies.

Health Canada believes Canadians must have a voice in the debate concerning how far we should go to save human life. In 2000, Dr. Einsiedel led a pilot consultation process in Calgary on the future of xenotransplantation. In 2001, she was involved in a small public consultation process in Edmonton. In this instance, 15 to 20 individuals were recruited from a random sample of residents to sit on a citizen jury. The jurors were provided with educational materials on xenotransplantation and were asked to attend a three-day forum to meet and question various experts on the issues surrounding this new technology. The consultation process came to be the model for the process Health Canada used to consult with citizens in Halifax, Quebec City, Toronto, Saskatoon, Vancouver, and Yellowknife to determine if animal organs should be used in transplant surgery when human organs cannot be found.

The Edmonton citizen jury responded with "a cautious yes" to clinical trials, however the Calgary citizens recommended a moratorium on clinical trials at this time, as did the majority of Canadians participating in the cross-Canada consultation process. Informed Canadians were deeply concerned about the risks of zoonotic disease (viruses transmitted from animals to humans) causing a large-scale epidemic among the general population. They were also nervous regarding the costs involved in xenotransplantation, the health risks posed to the individual patient, and the welfare of the animals being genetically engineered. They felt that the potential risks of xenotransplantation were greater than the potential benefits and concluded it was safer not to open Pandora's box at this time. They also recommended that a strong regulatory framework be established to oversee any future clinical trials.

Dr. Edna Einsiedel is Professor in the Graduate Program in Communications Studies at the University of Calgary. She was also a member of the Canadian Public Health Association's Public Advisory Group responsible for developing recommendations to Health Canada on xenotransplantation based on input from Canadians (September 2000 to March 2002). Dr. Einsiedel is supported by the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Recent publications

Einsiedel EF. Citizen voices: public participation on biotechnology. *B-Ethics* 2001; 1(3):93-104.

Einsiedel EF. Animal-spare parts? The Canadian public consultation on xenotransplantation. *Public Understanding of Science*. In press.

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The Genetics of Glaucoma

Glaucoma is one of the leading causes of blindness in Canadians. A fluid buildup in the chamber between the iris (the coloured part of the eye) and the cornea can lead to increased pressure on the entire eye, including the vulnerable optic nerve. Glaucoma is characterized by progressive degeneration of the optic nerve, often associated with this increased pressure. With as high a rate of frequency as heart disease, glaucoma is inherited in at least 50% of sufferers.

Heritage Senior Scholar Dr. Michael Walter has identified one of the genes that causes glaucoma—a gene called FOXC1. This gene turns other genes on or off during development, and mutations of the same gene can lead to dental, jaw, umbilical, and ocular defects. Dr. Walter is now working toward understanding how FOXC1 works, which other genes it controls and interacts with during development, and ultimately, why mutations of this gene cause glaucoma.

Dr. Walter explains that there are some very good treatments, both medical and surgical, for glaucoma. Initially, a patient would be started with medical treatments, such as eye drops, in hopes of reducing the pressure on the eye. If the medications don't work, surgery is tried. "We're hoping that by understanding the genetic basis of glaucoma, we will be better able to predict who will respond to medication and who will respond to surgery," Dr. Walter says, "because the faster we can treat glaucoma and get it under control, the more vision we can save."

GLAUCOMA IS INHERITED IN AT LEAST 50% OF SUFFERERS

FOXC1 is a rare cause of glaucoma and is responsible for less than 1% of all cases. The patients who have FOXC1 mutations are classified with a condition called Axenfeld-Rieger malformations—a constellation of eye, jaw, and dental symptoms. "We work on this relatively rare form of glaucoma in the hopes of understanding more about the more common types of glaucoma," explains Dr. Walter, one of only three molecular biologists in Canada doing genetic research on glaucoma. In another of his projects, Dr. Walter is working on identifying the causes of macular degeneration, the number one cause of blindness in North America.

Dr. Walter's work has not gone unrecognized. He recently received the Cogan Award from the Association for Research in Vision and Ophthalmology (ARVO), awarded annually to a researcher under the age of 40 who has made important contributions to research in ophthalmology or visual science directly related to disorders of the human eye. One of his students, Ramsey Saleem, has received the C. W. Cotterman Award from the American Society of Human Genetics for his work on FOXC1.

"As the population ages, we are becoming increasingly aware of age-related problems like glaucoma," says Dr. Walter. "If you live to the age of 90, you have almost a 90% chance of having vision loss from one of these conditions." He adds that anybody over the age of 40 should get a test for glaucoma every other year, and those with a family history of glaucoma should be checked every year. "Glaucoma is a debilitating disease and is going to cause increasing stress to our health system. If we can do something to prevent it, we really need to do it."

Dr. Michael Walter is a Heritage Senior Scholar and an Associate Professor in the Department of Ophthalmology and the Department of Medicine's Division of Medical Genetics at the University of Alberta. He also receives funding from the Canadian Institutes of Health Research (CIHR) and the Canadian Genetic Diseases Network.

Selected publications

Saleem RA, Walter MA. The complexities of ocular genetics. *Clinical Genetics* 2002 Feb;61(2):79-88.

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RIGHT: DR. MICHAEL WALTER

the heart of the matter

Have you ever worried about your blood pressure or cholesterol? Unfortunately, high blood pressure (hypertension), high cholesterol, diabetes, and other risk factors for heart disease are very common in our society. Even if your blood pressure and cholesterol are fine, you probably know friends, neighbours, relatives, or colleagues who have these risk factors. It's not surprising that the older we become, the more we tend to worry about developing cardiovascular disease.

Fortunately, **many excellent scientists and physicians in Alberta are working hard in this area, and their efforts to better understand the workings of the heart and blood vessels will enable them to better prevent and treat cardiovascular disease, helping us to live longer and better.**

Improving healthcare for patients with heart disease

At the University of Calgary, Heritage Population Health Investigator Dr. Kathryn King has drawn on her clinical and research experience in cardiology and cardiac surgery to develop a new study looking at how Canadians make decisions about their health. Dr. King is particularly interested in how gender and culture can affect heart patients' decisions regarding their care. For instance, our cultural background may influence eating habits or health beliefs, and gender issues can have an impact on recovery following cardiac surgery and rehabilitation. Dr. King is hoping her four-year study in risk management decision-making will one day lead to practical improvements in healthcare delivery for people with heart disease.

"We want to take a fresh look at appropriate models of care for cardiac patients. Ultimately, our goal is to be able to develop a decision-making model of care that is sensitive to both gender issues and ethnocultural affiliations," she explains. "Our existing models don't capture the essence of gender and culture as well as they could in today's society. It's important to try to understand a person's culture, and to work with it, both physically and from the psychosocial perspective."

Over the next few years, Dr. King's team of researchers will survey a thousand Canadians of all ages, from across Canada. The interviewees will include urban and rural Euro-Canadians and French Canadians, Chinese immigrants from Hong Kong, Sikhs, and aboriginal people living on reserves.

DR. KATHRYN KING

The risk for heart disease

Heritage Scholar Dr. Todd Anderson heads a Calgary research group that's investigating how to best assess and then address an individual's risk of heart disease. Dr. Anderson's team focuses specifically on the endothelium, the single-cell lining of blood vessels. They're looking at endothelial function in the coronary circulation (the movement of blood to heart muscle cells through the arteries) and the peripheral circulation (the movement of blood from the heart to various organs and limbs) in patients at risk for atherosclerosis (clogged arteries). He hopes that better knowledge of the evaluation and treatment of the risk factors for cardiovascular disease will lead to better prevention.

"We now know that the endothelium is important. It plays an integral part in the control of whether someone gets atherosclerosis or not," explains Dr. Anderson. "You can measure endothelial function, both in animals and in humans. Over the last two decades, we've discovered that endothelial function responds abnormally if cholesterol builds up in the artery, or even if an individual has risk factors like diabetes, high blood pressure, or smoking."

Current research studies in this area are focusing on improving vascular function, particularly in patients with diabetes, kidney failure, or high levels of cholesterol or atherosclerosis. For instance, Dr. Anderson and his colleagues are assessing the impact of demographic, biochemical, and genetic risk factors and how these factors interrelate, as well as how various new medications improve endothelial function.

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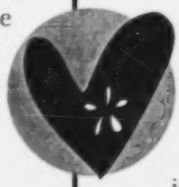
It's a dynamic process, he explains. The physician can improve endothelial function by prescribing medication to lower cholesterol, blood pressure medication (such as ace inhibitors), or anti-platelet drugs, or by modulating insulin resistance (with a drug called metformin).

Dr. Anderson is also the principal investigator in the ongoing "Firefighters and their endothelium" (FATE) clinical trial. About 1600 middle-aged male firefighters from Calgary and three other centres are participating in this eight-year study to assess the clinical usefulness of endothelium function tests in predicting whether an individual is at risk for a heart attack or stroke. One day you may go to your doctor's office to have your endothelial function assessed along with your blood pressure and cholesterol.



Working toward reducing stroke injury

Heritage Medical Scientist Dr. Paul Kubes is studying how and why white blood cells are recruited to sites of inflammation. One day his research could lead to ways to reduce the initial brain injury caused by stroke.

"Normally white cells fight infection," explains Dr. Kubes, Chair of the University of Calgary Immunology Research Group. "If you get a paper cut or an infection in your lungs, the white cells come, destroy the bacteria, and life goes on." However, in certain situations where there is reduced blood flow (ischemia), as in a stroke or heart attack, a flood of white cells will appear even though there is no infection. When blood flow returns to normal, the white cells recognize that the tissue is different. They decide to remove it and start anew. In the case of brain or heart tissue, this action results in significant injury.

In a stroke or heart attack, a flood of white cells will appear even though there is no infection.

"What we're trying to figure out is how the white cells get into these tissues and if we can come up with strategies to prevent them getting there," he explains. "Part of the problem is that we really don't have a clear understanding how the white cells get out of the blood vessels. They move at incredibly high speeds, and then they suddenly stop." He adds that since different organs use very different mechanisms of white cell recruitment, a better understanding of the heart's recruitment process is needed before those white cells can be targeted and studied.

Trying to prevent sudden death

Calgary cardiologist and Heritage Clinical Investigator Dr. Derek Exner has a special interest in the risk factors and therapies for serious heart rhythm problems. Dr. Exner is involved in a variety of cardiovascular clinical trials investigating why heart attack patients are more likely to die from sudden cardiac death due to heart rhythm problems than those who have not had a heart attack. Based on studies elsewhere, it's estimated about 3000 to 3500 Albertans fall prey to sudden cardiac death annually. Many will have had a prior heart attack.

Dr. Exner is assessing how a heart attack affects the heart's electrical system and the autonomic nervous system that controls the heart, as well as the impact of depression on the autonomic nervous system. He hopes that one day the results of his research will help identify people at risk before they start to develop problems, so that measures can be taken to lower their risk and prevent deaths.

In May 2001, Dr. Exner and colleagues at teaching and community hospitals in Calgary and Edmonton began recruiting 350 Albertans to participate in a four-year clinical trial. They're enrolling heart-attack survivors, aged 30 to 90, who have some measurable damage to the heart muscle. The study aims to identify which patients will develop heart rhythm problems, and to determine when and how often testing should be undertaken following a heart attack. Each participant will undergo three different sets of tests, during which researchers will measure any impact on the patient's autonomic nervous system and whether the electrical system of the participant's heart was affected by the heart attack.

LEFT: DR. PAUL KUBES. ABOVE: DR. TODD ANDERSON

Dr. Exner aims to develop a more widely applicable, non-invasive way of undertaking cardiac assessments.

Currently, these tests for heart patients are invasive and only available in major centres. Dr. Exner aims to develop a more widely applicable, non-invasive way of undertaking cardiac assessments so that patients in smaller centres can also be tested. He estimates that all the patients will be enrolled in this study by July 2003, and the final results will be published in 2005.

Dr. Exner points out that one of the major challenges has been to find patients with obvious heart damage, given the high quality of care for patients with a heart attack. "Cardiology in Alberta is certainly comparable to anywhere else in North America and probably superior to many sites," he says.

Discovering who is likely to have a stroke early in life

Heritage Scholar Dr. Sarah Childs is investigating the genes involved in angiogenesis, the process by which new blood vessels develop. In several diseases, angiogenesis is increased, while in others it can be impaired. Other studies related to this topic suggest that knowledge of the genes controlling blood-vessel growth may lead to new treatments for various health problems, including stroke and cancer.

"We're trying to identify the genes that specifically influence the way blood vessels develop," says Dr. Childs, a member of the University of Calgary Smooth Muscle Research Group. "For instance, we would like to identify the genes that predispose infants to have strokes. With all the information we now have from genome projects, we're just on the edge of being able to discover a lot of connections that have been really difficult to make before. We now need to focus on what's the best question to ask."

Dr. Childs is using the zebrafish, a small, tropical fish, to investigate early growth of blood vessels.

ABOVE: DR. DEREK EXNER

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Easing children's pain — the heart as a reference

Edmonton anesthesiologist and AHFMR Clinical Investigator has developed an effective new epidural technique, the "Tsui test", for controlling pain during and after surgery.

Anesthesiologists often use epidural anesthesia to control a patient's pain a technique that has long been used in childbirth, for instance. Dr. Tsui has designed a new way of delivering epidural pain control that's easier and safer to use in challenging cases, such as lung transplant patients, and small babies and young children (under three years of age) undergoing major chest or stomach surgery. The patented Tsui test has a success rate of about 90% (as compared to 50% previously).

"With the epidural, we can control pain better," says Dr. Tsui. "Before, if a child was crying we had no idea if they were in pain, hungry, or there was another reason. With this we know exactly where we are."

Dr. Tsui uses a small, flexible epidural catheter to deliver the local anesthesia to the specific part of the infant's body that needs freezing. He threads the catheter tip from the caudal space in the tailbone area up to the higher level of the body where pain control is needed. He uses the child's heart as a reference point to help him determine the location of the catheter tip following insertion and to guide its final placement.

"Pilots know how far the plane is away from an airport because they pick up the signals from the control tower," he explains. "When they get closer to the airport, they receive different signals. When the catheter is high in the body and closer to the heart, we also receive different signals, better signals."

Children receiving epidural anesthesia this way are less likely to need morphine, and are therefore less likely to end up on a ventilator in Intensive Care for several days following surgery.

Dr. Ban Chi-Ho Tsui is an AHFMR Clinical Investigator and also receives Research Excellence Envelope funding from the University of Alberta Faculty of Medicine. He is an Assistant Professor in the Department of Anesthesiology and Pain Medicine.

Recent publication

Tsui BCH, Seal R, Koller J. Thoracic epidural catheter placement via the caudal approach in infants by using electrocardiographic guidance. *Anesthesia & Analgesia* 2002 Aug;95(2):326-330.

"We're trying to identify the genes that specifically influence the way blood vessels develop."

Zebrafish have a number of advantages for her research: their cardiovascular system is very similar to that of mammals; they produce a large number of eggs each week; and their embryos are transparent. This transparency allows her to observe the embryos' blood vessels and blood cells by microscopy to learn more about the earliest stages of development of blood vessels. It also allows Dr. Childs to perform very detailed screens for subtle genetic defects affecting vessel development.

The U of A Vascular Biology Research Group

Members of the University of Alberta Vascular Biology Research Group—Drs. Stephen Archer, Evangelos Michelakis, and Jason Dyck—enjoy a "translational" approach to research, taking an idea all the way from the laboratory bench to the patient's bedside.

Heritage Scientist Stephen Archer, a basic scientist as well as a cardiologist, has a special interest in pulmonary circulation and "oxygen sensing." All mammals, including humans, are designed to live with a certain oxygen level in their blood, he explains. They all have sensors in the blood vessels that monitor oxygen levels in the lung. These sensors detect when oxygen levels alter, just as a thermostat detects temperature changes in a home. When the oxygen level falls (such as in pneumonia, altitude sickness, or a collapsed lung following surgery), the body senses that and reacts to keep the oxygen uptake normal. The lung is not the only oxygen-sensitive organ in the body. There are also oxygen sensors in the blood vessels, in the airways of the lung, in the human placenta, and in the adrenal glands of babies.

Dr. Evangelos Michelakis, a Heritage Scholar, also has expertise in both basic science and clinical research. Recruited to Edmonton after completing his internal medicine and cardiology training at Yale University and the University of Minnesota, Dr. Michelakis suggests that the strong partnership between the university and AHFMR fosters excellent bench-to-bedside research in Alberta. In the case of the Vascular Biology Research Group, researchers first investigate in animals treatments based on gene therapy or *de novo* drug approaches to treat pulmonary hypertension. If this preclinical animal research proves successful, they then apply these findings in clinical trials with human patients.

In 2001, Dr. Michelakis established the Cardiovascular Ion Channel Gene Therapy Unit (CIGNET) at the University of Alberta. Funded by the Canada Foundation for Innovation and the Government of Alberta's Innovation and Science Research Investment Program, CIGNET uses cutting-edge basic science technologies to determine the role of ion channels in cardiovascular physiology.

Another member of the Vascular Biology Group is Heritage Scholar Dr. Jason Dyck, a molecular biologist. Dr. Dyck received his B.Sc. and Ph.D. from the University of Alberta, then did post-doctoral work at Baylor College of Medicine in Houston and at Dartmouth Medical School in New Hampshire before being recruited back to Edmonton. Also a member of the CIHR Cardiovascular Research Group and the Perinatal Research Centre, Dr. Dyck has expertise in gene transfer and adenoviral gene delivery techniques, and is currently studying cardiac energy metabolisms and cardiac hypertrophy, an enlargement of the heart that often precedes heart failure.

"What we're trying to do is make the heart work as efficiently as possible, to optimize its use of energy," explains Dr. Dyck. "Our primary focus is to identify and characterize proteins that regulate cardiac energy metabolism at the cellular level." The next step is

ABOVE: DR. SARAH CHILDS

RIGHT: (L TO R) DRS. EVANGELOS MICHELAKIS, STEPHEN ARCHER, JASON DYCK AND BERNARD THEBAUD, A NEW MEMBER OF THE RESEARCH GROUP

to take the gene that codes for the specific protein and genetically engineer a virus that can efficiently deliver the gene to the heart. The virus is infused into a rat heart. Several days later, once the protein is expressed, the heart is removed and analyzed for changes in energy metabolisms.

"In this way, we can see if we have actually changed the heart's energy preference and how well the heart functions with these changes. In addition, we can test whether the gene can protect the heart from ischemic injury that is often associated with heart attacks or open-heart surgery. If the genes that we're interested in turn out to be beneficial, then that would be the first step on the road to a gene therapy."

Trying to prevent premature death

Drs. Archer, Michelakis, and Dyck recently pooled their knowledge and expertise in basic science and clinical practice to develop a new treatment for pulmonary arterial hypertension (PAH). "Our research varies from quite basic (such as cloning genes and putting them into viruses) to applied research, like taking a drug (Viagra) that's clinically available and trying to treat pulmonary hypertension," explains Dr. Archer. PAH is a relatively rare but very serious disorder of the blood vessels of the lungs. The blood pressure in the arteries of the lung rises very high, placing a huge strain on the right chamber of the heart. PAH eventually causes heart failure and premature death.

ABOVE RIGHT: DR. JASON DYCK

Drs. Archer, Michelakis, and Dyck recently pooled their knowledge and expertise in basic science and clinical practice to develop a new treatment for pulmonary arterial hypertension (PAH).

Drs. Archer, Michelakis, and Dyck were the first to show that a single dose of sildenafil (Viagra), a drug ordinarily used to treat erectile dysfunction, significantly lowers blood pressure in PAH. Viagra seems to be a safe, effective medication for patients with this vascular disorder. It's also less costly and is associated with fewer side effects than existing treatments for PAH. The Edmonton team is now undertaking a new clinical trial to discover if Viagra remains effective in PAH over the long term.

The Canada Foundation for Innovation has provided funding to construct a new $17 million Heart and Stroke Research Centre in Edmonton. Under the direction of Dr. Archer, this centre will enable the University of Alberta's clinician-scientists to collaborate with basic scientists to study heart disease and stroke in a world-class facility.

Dr. Kathryn King is a Heritage Population Health Investigator and also receives funding from the Canadian Institutes of Health Research (CIHR) and the Social Sciences and Humanities Research Council of Canada (SSHRC). She is an Associate Professor, holding a joint appointment in the Faculty of Nursing and in the Faculty of Medicine's Department of Community Health Sciences, at the University of Calgary.

Dr. Todd Anderson is a Heritage Scholar. He also receives funding from the Heart and Stroke Foundation of Canada, CIHR, and the Canadian Diabetes Association, as well as physician-initiated grants from Pfizer Canada, Eli Lilly, GlaxoSmithKline, Aventis, and Calgary Laboratory Services. He is an Associate Professor in the Department of Medicine at the University of Calgary.

Dr. Paul Kubes is a Heritage Scientist and a Canada Research Chair. He also receives funding from CIHR, the Bayer Partnership Fund, and the Heart and Stroke Foundation of Canada. He is a Professor in the Department of Physiology and Biophysics and the Department of Medicine at the University of Calgary.

Dr. Derek Exner is a Heritage Clinical Investigator and a CIHR Clinician Scientist who also receives funding from the Heart and Stroke Foundation of Canada. He is an Assistant Professor in the University of Calgary departments of Medicine and Community Health Sciences.

Dr. Sarah Childs is a Heritage Scholar and also receives funding from the Heart and Stroke Foundation of Canada and the Canadian Institutes of Health Research. She is an Assistant Professor in the Department of Biochemistry and Molecular Biology at the University of Calgary.

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the heart of the matter

Dr. Stephen Archer is a Heritage Scientist and also receives support from CIHR, the Heart and Stroke Foundation of Alberta, and the Canada Foundation for Innovation. He is a Professor in the departments of Medicine and Physiology at the University of Alberta, Director of the Division of Cardiology, and Heart and Stroke Foundation Chair in Cardiovascular Research for Northern Alberta, NWT, and Nunavut.

Dr. Evangelos Michelakis is an AHFMR Scholar and a CIHR New Investigator. He was the Canadian Cardiovascular Society Young Investigator for 2001. He holds funding from CIHR, the Heart and Stroke Foundation, the Canada Foundation for Innovation, and the Alberta government's Medical Services Innovation Fund. An Assistant Professor in the Department of Medicine (Cardiology), he is the Director of the University of Alberta Pulmonary Hypertension Program, as well as of the Cardiovascular Ion Channel Gene Therapy Unit (CIGNET).

Dr. Jason Dyck is a Heritage Scholar whose research is also supported by the CIHR and the Heart and Stroke Foundation of Canada. He is an Assistant Professor in the University of Alberta Department of Pediatrics and Child Health and the Department of Pharmacology; Director of the CIHR-supported U of A Viral Core Facility; and a member of the university's Cardiovascular Research Group and the Vascular Biology Research Group.

Recent publications

King KM, Humen DP, Smith HL, Phan CL, Teo KK. Psychosocial components of cardiac recovery and rehabilitation attendance. *Heart* 2001 Mar;85(3):290-294.

Mather KJ, Verma S, Anderson TJ. Improved endothelial function with metformin in type 2 diabetes mellitus. *Journal of the American College of Cardiology* 2001 Apr;37(5):1344-1350.

Ibbotson GC, Doig C, Kaur J, Gill V, Ostrovsky L, Fairhead T, Kubes P. Functional alpha4-integrin: a newly identified pathway of neutrophil recruitment in critically ill septic patients. *Nature Medicine* 2001 Apr;7(4):465-470.

Veenhuyzen GD, Singh SN, McAreavey D, Shelton BJ, Exner DV. Prior coronary artery bypass surgery and risk of death among patients with ischemic left ventricular dysfunction. *Circulation* 2001 Sep;104(13):1489-1493.

Childs S, Chen J-N, Garrity DM, Fishman MC. Patterning of angiogenesis in the zebrafish embryo. *Development* 2002 Feb;129(4): 973-982.

Michelakis E, Tymchak W, Lien D, Webster L, Hashimoto K, Archer S. Oral sildenafil is an effective and specific pulmonary vasodilator in patients with pulmonary arterial hypertension: comparison with inhaled nitric oxide. *Circulation* 2002 May;105(20):2398-2403.

Soltys C-LM, Buchholz L, Gandhi M, Clanachan AS, Walsh K, Dyck JRB. Phosphorylation of cardiac protein kinase B is regulated by palmitate. American *Journal of Physiology: Heart and Circulatory Physiology* 2002 283(3):H1056-H1064.

Burning questions

"The last patient to have *P. aeruginosa* had left the Unit a month before Mr. Shaw was admitted," explains Dr. Tredget. "The Burn Unit had been closed completely over the Christmas season, yet the bacteria were still there. We needed to find out why."

Through some detailed medical detective work involving molecular biology typing, Dr. Tredget's team was able to find the culprit. The bacteria were living in the hydrotherapy unit, which was used to clean burn wounds. Despite strict procedures to clean the unit, bacteria were able to stay alive in its piping system. The hydrotherapy tub was immediately removed.

But eliminating hydrotherapy was not a complete solution. Hydrotherapy was needed to wash creams off wounds before they were reapplied. Those creams contain silver, which is a powerful antimicrobial and bactericidal agent. The Firefighters' Burn Treatment Unit switched to a silver nitrate solution, which did not need to be washed off.

Now another problem emerged: silver nitrate causes black stains and made a mess in the Unit. That spurred the researchers to develop a new kind of dressing that released a controlled dosage of silver nitrate directly into the wound. Developed in conjunction with the

But eliminating hydrotherapy

Part of this work involves growing an artificial skin.

Westaim Corporation, based in Fort Saskatchewan, Acticoat is now a product of Westaim Corporation subsidiary NUCRYST Pharmaceuticals, and is marketed and sold by Smith & Nephew.

"Doing without hydrotherapy was a revolutionary idea," notes Dr. Tredget. "Since we published our research, centres around the world have either stopped using hydrotherapy or significantly reduced its use. This may seem like a lot of effort for one case of infection, but in the end this work has helped many, many people. That's the great advantage of having a research capability in addition to looking after patients. You're not limited to what you read in a book or whatever medicine you can buy. We see unusual problems, and we try to find solutions."

One of the solutions Dr. Tredget is looking for is a treatment for a type of excessive scarring called hypertrophic scarring. About 30% of patients admitted to burn units, and up to 60% of burn patients under the age of 5, develop this complication. Hypertrophic scarring is disfiguring, painful, and psychologically devastating, and it affects the quality of life for many burn patients.

Dr. Tredget's research team has made a number of advances in understanding the scarring process. They are now developing innovative treatments using results from their basic research on the underlying mechanism that causes scarring.

The research team focuses on a group of proteins, known as fibrogenic growth factors, which are overexpressed in burn patients and promote the development of hypertrophic scarring. One of the most important of these is transforming growth factor beta 1 (TGF-β1). Effective treatment will almost certainly depend on figuring out how to block the production of TGF-β1. The team has developed a promising approach that uses interferon alpha to normalize the expression of TGF-β1. The Burn Unit is in the midst of a Phase 3 clinical trial of this therapy.

In other research, the University of Alberta team is investigating ways to manipulate healing by engineering skin grafts to include various growth factors. Part of this work involves growing an artificial skin, a project that has just begun. Collaborators include Dr. Aziz Ghahary, Associate Professor in the Department of Surgery, and Dr. Paul Scott, Professor in the Department of Biochemistry.

"We're working on a number of fronts on the molecular level," says Dr. Tredget. "It's a substantial research effort—our research funding at the Burn Unit amounts to about $1.3 million per year. Our ultimate goal is to speed up post-burn wound healing and at the same time avoid the development of hypertrophic scarring.

"This is exciting work, but it's not enough. If all I'd done with my career is focus on wound-healing research—which I could have—we'd still have patients dying of *P. aeruginosa* infections in the Burn Unit. As a doctor, I must also focus on helping my patients, and they need help immediately. So I do both research and patient care, and there's a synergy between them. Above all, we're looking for results."

Dr. Tredget is a Heritage Senior Scholar and a Professor in the Department of Surgery at the University of Alberta. His work is also supported by the Firefighters of Alberta, the International Association of Fire Fighters Burn Foundation, and the Canadian Institutes of Health Research (CIHR).

Selected publication

Tredget EE, Shankowsky HA, Joffe AM, Inkson TI, Volpel K, Paranchych W, Kibsey PC, Alton JD, Burke JF. Epidemiology of infections with Pseudomonas aeruginosa in burn patients: the role of hydrotherapy. *Clinical Infectious Diseases* 1992 Dec;15(6): 941-949.

was not a complete solution.

A FAMILY BUSINESS

SUCCESS STORY

In the business world, where growth is often valued more than any other attribute, a Red Deer entrepreneur has bucked the trend and achieved success by staying small.

Carol White, a former nurse and upholsterer, began a specialty wheelchair seating business in 1993. The idea had been brewing for some time while White ran a wheelchair sales and service business. She saw that the design and manufacture of custom seating could be a business on its own—one that would allow her some creativity and a chance to use her upholstery skills. It was the start of Innovators 1993 Inc.

The company's first product was the K-Special Back, a wheelchair back that improves the seating and positioning of patients with curvature of the spine (known as kyphosis). Kyphosis may develop in later life as a result of osteoporosis. As the bones of the spine weaken and thin, they begin to deteriorate and compress upon each other. The result is a "dowager's hump". Sitting in a wheelchair can exaggerate this condition, and make sitting very uncomfortable.

White recognized that a wheelchair back shaped to accommodate the curvature would enable a more erect seating position and therefore a more functional head position—eyes forward, not looking toward the ground.

The K-Special Back went into clinical trials with occupational and physical therapists in the Red Deer region in 1993. At the same time, White proceeded to secure patents for the product. During discussions with a patent agent, AHFMR's Technology Commercialization (TC) program was mentioned as a resource to assist Albertans with the transfer of new ideas and scientific findings into successful commercial health products and processes. White applied for TC funding, and Innovators received $75,000 in 1994. The money helped the company develop a business plan, investigate distribution channels, train sales representatives, and expand its Red Deer manufacturing facility.

"The TC funding helped us in the early stages of the company," says White. "It wasn't the difference between success and failure, but it certainly eased our financial situation. As a result, we moved quicker with the product than we would have on our own."

Innovators now manufactures a wide range of wheelchair support products—about 60 of them, all designed by White—including trays, backs, and bolsters. Approximately 80% of sales are in Ontario. Innovators has also been building a relationship with an American distributor, and sales are commencing in the United States.

The company has done well, with sales growth averaging in excess of 15% annually. The revenue allowed Innovators to repay its loan from the TC program, the final payment being made in August of this year. Innovators is the first company in 17 years to pay back its loan to AHFMR.

The pay-back attracted considerable media attention. White notes that one reporter wanted to know why she bothered to pay it back, since the loan was interest-free. "I was a bit taken aback by the question," she says. "I said I would pay it back, so of course I did."

The answer characterizes White's approach to business: honest and straightforward. "Our focus has always been on unique products that perform exactly as intended. We've earned a reputation for quality.

INNOVATORS NOW MANUFACTURES A WIDE RANGE OF WHEELCHAIR SUPPORT PRODUCTS.

"Sure, we could expand our line far beyond 60 or so products, but that wouldn't guarantee us more profit—just more work. I'm a conservative person. 'Bigger is better' is not my philosophy. We've made a con-

scious decision to keep things manageable, stay in our niche and maintain our reputation."

This philosophy is behind Innovators' decision to maintain a modest central manufacturing facility. Five people work in the central office and six others run subsidiary shops out of their homes. The subsidiary shops make a variety of components; final assembly is done in the central office.

"I wanted to structure the company so that work was convenient and efficient," adds White. "Allowing people to work at home, rather than expecting them to leave their young children and come to work, just makes sense."

In 2000, White handed over day-to-day management to her son, Gordon. She now works exclusively on product design, and has time to enjoy her 10 grandchildren.

"My vision was a family business, and we have a number of family members working with us. But just having family around doesn't guarantee a family atmosphere. By staying fairly small we've been able to create a good working environment for all staff. It has made Innovators a successful business and a good place to work."

chronic pain management

As the joke goes, a doctor sees a patient hitting himself in the head with a hammer. The doctor asks, "Why are you doing that?" The patient replies, **"Because it feels so good when I stop."**

But what if the pain doesn't stop? This is chronic pain, a condition that currently offers more questions than answers. What is it? What causes it? What is the best way to manage it? Chronic pain can be as much an enigma to health professionals as it is to sufferers.

"What we do know is that chronic pain is a serious public health issue," says Dr. Paul Taenzer, a psychologist and Clinical Service Manager for the Calgary Chronic Pain Centre. "In Alberta we have highly specialized pain clinics in both Calgary and Edmonton, but the need for effective chronic pain management is much greater than these clinics can provide. As a result, many Albertans suffer from chronic pain and do not receive optimal care. What's needed is a much larger strategy to deal with chronic pain."

And what is the best way to manage chronic pain? "We don't have the answer to this question," continues Dr. Taenzer. "There

management

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ABOVE: DR. PAUL TAENZER

"What's needed is a much larger strategy to deal with chronic pain."

are a lot of published reports about what works and what doesn't. There are clinicians like myself who are passionate about a particular approach. But what's missing is a comprehensive analysis of available data on the treatment of chronic pain."

The need to find effective treatment approaches for Albertans with chronic pain has been recognized by Alberta Health and Wellness, which in partnership with the Alberta Medical Association, the Capital Health Authority, and the Calgary Health Region, initiated pilot projects to evaluate the effectiveness of comprehensive "multidisciplinary chronic pain programs" in Edmonton and Calgary. In multidisciplinary chronic pain management, people suffering from chronic pain work with a team of professionals, including medical specialists and rehabilitation professionals, who reduce the burden of pain, help the person learn to cope more effectively with the remaining pain, and assist them in improving their functioning in day-to-day life.

Another key player in the effort to improve care for people with chronic pain in Alberta is the Health Technology Assessment (HTA) Unit of the Alberta Heritage Foundation for Medical Research. The HTA unit evaluates the properties and effects of health-care technology and provides research for health-care decisions.

An information-sharing group, chaired by Dr. Taenzer, was created to provide population data and research evidence on chronic pain. It includes Dr. Don Schopflocher and Henry Borowski from Alberta Health and Wellness, Dr. Saifee Rashiq from the Department of Anesthesiology and Pain Medicine at the University of Alberta, and Christa Harstall and Maria Ospina from the HTA Unit at the AHFMR.

"We're very fortunate to have the HTA Unit working with us," says Dr. Taenzer. "They bring an authoritative structure for looking at research results."

Christa Harstall, Assistant Director of the HTA Unit, adds, "This is an important project, and Alberta has an opportunity to break some new ground. We've got a spectacular team with an amazing breadth of skills. The group is eager to be informed by the empirical evidence."

One of the first tasks has been to collect baseline information on the prevalence of chronic pain. Ms. Harstall notes that while there are many studies available, they often define chronic pain differently, making comparisons difficult. The HTA Unit is also analyzing studies that have evaluated the outcomes of multidisciplinary pain-management programs. Pending approvals, the team may extend the study to look at funds expended on pain management in Alberta.

While much of the study is focused on the multidisciplinary management of chronic pain, the group is also considering looking at outcomes of single-modality treatments. This information would particularly help rural physicians who don't have access to the teams of pain-management professionals that are available in the cities.

"The bottom line is that people continue to suffer from chronic pain despite our best intentions," Dr. Taenzer notes. "This project is exciting because it will bring some clarity to our understanding of chronic pain, so we can ultimately do a better job of helping patients."

Looking at dots

Darrin Lindhout looks at dots all day long—or at least that's how he sometimes explains the complexities of his Ph.D. project in biochemistry.

Darrin is working on identifying the structure of a human cardiac protein complex–troponin C and troponin I–using nuclear magnetic resonance (NMR) spectroscopy. These proteins play a vital role in maintaining the normal function of the heart. "Troponin C is basically the quarterback of muscle contraction," Darrin explains. "It initiates the start of each heartbeat."

The dots Darrin looks at are generated when a protein is dissolved in a solution and placed in an NMR magnet to produce a spectrum of the amino acids within the protein. These dots give the information needed to produce structural images of the protein. NMR also allows Darrin to see the dynamics of these proteins–how they behave, move, and interact with one another in the solution.

Darrin's studies of troponin C and troponin I have also allowed him to apply his work to a genetic disorder called familial hypertrophic cardiomyopathy, involving an enlargement of the left ventricle of the heart which can cause sudden cardiac impairment and death. "You sometimes hear of an athlete who exhibits no sign of heart trouble and then goes out for a run one day and drops dead of a heart attack, which is later found to have been caused by this condition," Darrin explains. Hypertrophic cardiomyopathy arises from mutations in heart proteins, and one of these mutations occurs in the region of troponin I that Darrin has been studying, allowing him to examine it for abnormalities. The mutant troponin I (R145G) binds to troponin C at only a quarter of the strength of the regular troponin I. Since troponin C initiates

NMR also allows Darrin to see the dynamics of these proteins.

This weaker binding explains the resulting problems with the heart's ability to contract properly.

heart contraction, this weaker binding explains the resulting problems with the heart's ability to contract properly.

Another of Darrin's research interests has involved examining what occurs in a region of troponin I after a heart attack. He explains that following a heart attack, cells of the heart are under incredible stress due to the possibility of oxygen starvation, nutrient depletion, and cellular damage. The stressed condition of the cells can cause phosphate groups to bind to specific amino acids within troponin I. This phosphorylation of troponin I leads to a protein interaction with troponin C that is only 1/14 the strength of the normal interaction. The weaker binding with the protein that initiates the heartbeat impairs the heart's ability to function properly following a heart attack.

A native of Red Deer, Darrin plans to pursue a post-doc after he completes his Ph.D., and then either continue in academia or make the jump to industry. He cites the mentorship and friendship of Dr. Brian Sykes and the relaxed and enjoyable atmosphere created by colleagues in the lab as key factors in his work. "They make it a lot of fun. If you're going to be in a lab for four or five years, you'd better get along with your co-workers," he says with a grin.

With the support of a Heritage Studentship, Darrin Lindhout is working on a Ph.D. in biochemistry at the University of Alberta under the supervision of NANUC (National High Field Nuclear Magnetic Resonance Facility) Director Dr. Brian Sykes.

Recent publication

Lindhout DA, Li MX, Schieve D, Sykes BD. Effects of T142 phosphorylation and mutation R145G on the interaction of the inhibitory region of human cardiac troponin I with the C-domain of human cardiac troponin C. *Biochemistry* 2002 Jun 11;41(23):7267-7274.

reader resources

Biocomputing: pictures worth many thousands of words

University of Calgary Biocomputing Group
http://moose.bio.ucalgary.ca/

Xenotransplantation: a Pandora's box?

University of Calgary Faculty of Communications and Culture
http://www.ucalgary.ca/UofC/faculties/COMCUL/

Health Canada: Report of the Xenotransplantation Surveillance Workshop
http://www.hc-sc.gc.ca/pphb-dgspsp/publicat/ccdr-rmtc/01vol27/27s1/index.html#contents

The genetics of glaucoma

The Glaucoma Foundation
http://www.glaucomafoundation.com/

Glaucoma Research Foundation
http://www.glaucoma.com/

The heart of the matter

Dr. Kathryn King's web page
http://www.ucalgary.ca/NU/scholarly/king.htm

Dr. Todd Anderson's web page
http://www.ucalgary.ca/smrg/anderson.htm

Dr. Paul Kubes' web page
http://www.ucalgary.ca/~girg/kubes.htm

Dr. Sarah Childs' web page
http://www.ucalgary.ca/smrg/sarah.htm

University of Alberta Vascular Biology Research Group
http://cardiosrv1.uah.ualberta.ca/vbrg/title.html

Easing children's pain—the heart as a reference

University of Alberta Department of Anesthesiology and Pain Medicine
http://www.med.ualberta.ca/departments/anesthesiology/

Burning questions

Firefighters Burn Treatment Society Edmonton Chapter
http://www.firefighterbtu.net

Chronic pain management

Calgary Chronic Pain Centre
http://www.crha-health.ab.ca/ccpc/

AHFMR Health Technology Assessment Unit
http://www.ahfmr.ab.ca/hta/

Looking at dots

Knowdeep Database: hypertrophic cardiomyopathy
http://www.knowdeep.org/cardiomyopathy/

2002 AHFMR Media Fellows

Theresa Wu

Biological Science and Psychology student, University of Calgary

I have always wanted to be a doctor, but there is something intriguing about the world of media that has always kept me questioning my career choice. When I saw the offer for the Media Fellowship through the AHFMR, I knew it was the perfect opportunity to answer my questions.

At CBC Radio, I found out that things that are absolutely fascinating to me are not always interesting to the general public. Neurotransmission, apoptosis, and immune responses may be appealing to a science student, but the typical media consumer would much rather hear about Parkinson's disease, cancer, and food allergies. To be a reporter is to communicate an important message to the general public in a way that they will find interesting and easy to understand—not to analyze something down to the atom. It's a skill that every medical professional should have in order to better relate to the public, and I am so glad that I got a head start.

The experience as a medical reporter was so fantastic, I was almost ready to give up my dreams of being a physician, and jump into the world of journalism—almost ready, but not quite. I was given a rare opportunity to sample a different career before plunging headfirst into my future. I am now certain of my choice to pursue a career in medicine, and am determined to keep one foot in the world of journalism by staying on as a freelance reporter with CBC so that I can maintain my skills.

Francesco Mosaico

Medical student, University of Alberta

Researching and reporting on emerging medical issues helped me to learn more about my own chosen profession. As I am considering specialization in public or community health, having some media savvy will be invaluable.

The highlight of my stay at CBC Radio was the airing of a 5-minute documentary I had prepared and voiced. It was played locally, and then sent to syndication and played across Canada in almost every major centre. The story followed a 52-year old Edson resident who had stuttered his whole life through an intensive 3-week clinic—from which he emerged speaking fluently.

I've been invited to continue freelancing with CBC Radio and time permitting, I hope to do so.

For more information on AHFMR's Media Fellowship program go to www.ahfmr.ab.ca/communications/fellowship.ahtml

TOP: THERESA WU BOTTOM: FRANCESCO MOSAICO

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2002 AHFMR Media Fellows

Theresa Wu

Biological Science and Psychology student, University of Calgary

I have always wanted to be a doctor, but there is something intriguing about the world of media that has always kept me questioning my career choice. When I saw the offer for the Media Fellowship through the AHFMR, I knew it was the perfect opportunity to answer my questions.

At CBC Radio, I found out that things that are absolutely fascinating to me are not always interesting to the general public. Neurotransmission, apoptosis, and immune responses may be appealing to a science student, but the typical media consumer would much rather hear about Parkinson's disease, cancer, and food allergies. To be a reporter is to communicate an important message to the general public in a way that they will find interesting and easy to understand—not to analyze something down to the atom. It's a skill that every medical professional should have in order to better relate to the public, and I am so glad that I got a head start.

It was a great feeling to know that the knowledge I have gained through university was being put to use, and the fact that I was the only reporter at CBC with a background in biology gave me the advantage of being sent to cover all the science-related stories. I had the chance to speak to some of the brightest minds in the medical world, and got a first-hand glimpse at the cutting-edge research going on in our own backyard.

The experience as a medical reporter was so fantastic, I was almost ready to give up my dreams of being a physician, and jump into the world of journalism—almost ready, but not quite. I was given a rare opportunity to sample a different career before plunging headfirst into my future. I am now certain of my choice to pursue a career in medicine, and am determined to keep one foot in the world of journalism by staying on as a freelance reporter with CBC so that I can maintain my skills.

Francesco Mosaico

Medical student, University of Alberta

Moving from the world of medicine to the world of journalism required learning a new vocabulary, practising new writing skills, and seeing issues and events from a "media" perspective, to name just a few adjustments.

Researching and reporting on emerging medical issues helped me to learn more about my own chosen profession. As I am considering specialization in public or community health, having some media savvy will be invaluable.

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